COMMENTS

Applicants appreciate the ability to respond to the newly provided prior art without the specter of final rejection looming. Many of the arguments noted below were also discussed at a personal interview earlier this year and, it is believed, were then considered to be persuasive. Nevertheless, applicants will supplement those arguments below to again achieve allowance of the application.

First, applicants would like to emphasize certain limitations found in the claims in this specific application and explain below how those particularly selected words define a claimed invention that is neither disclosed nor suggested in any of the cited references.

In particular, the variation of the inventive concept currently claimed in this application requires testing of "neural or muscle tissue samples." These samples are specific types of tissue. The claims do not recite a generalized tissue type. The claimed testing must be done to determine a "chronic effect' rather than merely the instantaneous effect that might otherwise be detected. Finally, the claimed method specifically requires the measurement of "the electrical properties of the neural or muscle tissue sample." That is to say that although all types of fluids may be present all about the specified tissue samples, the electroactivity of the sample itself is measured, not the secondary effects (e.g., pH) perhaps found in that surrounding liquid or medium.

Having made these few preliminary comments relating to the specific requirements of the claims, the references cited in the Office Action may now be discussed.

35 U.S.C. § 112, Second Paragraph -- Indefinite

Claims 12, 14, and 16 stand rejected under 35 U.S.C. § 112, second paragraph, as being vague and indefinite for the recitation of "chronic effect." The Office Action inquires of what "are the metes and bounds of chronic effect?" and further suggests that "As claimed, it is impossible to determine the metes and bounds of the claimed invention."

Applicants respectfully disagree. The meaning of "chronic" is a functional term well recognized in these arts. It is, for instance, specified in the attached copy of Stedman's Medical Dictionary as one "lasting a long time." Obviously, a "long time' is not a period identified in terms of a particular number of days, but it is terminology that is used in this technology to differentiate by comparison from instantaneous or short term effects.

Although applicants believe that the term as found in the claim is quite clear and are desirous of leaving it as it is, applicants would be amenable to broadening the claims to eliminate the term from the independent claim. If the Examiner would like to have the term eliminated, applicants ask that she contact applicant's attorney at the number listed below.

Meanwhile, withdrawal of the rejection is respectfully requested.

35 U.S.C. § 102(b) - Parce et al.

Claims 12, 14, and 16 stand rejected under 35 U.S.C. § 102(b) as anticipated by Parce et al. (U.S. Patent No. 5,278,048). In support of the rejection, the Office Action provides:

> "Parce et al. discloses a method of testing cell affecting agents (i.e., chemical substances) on living cells (i.e., neural of muscle tissue contains living cell; examiner is view a collection of similar cells as tissue). this method also discloses testing drugs on cells by measuring the pH by using semiconductor electrode (see claims). It is inherent that this method uses

at least two electrodes (i.e., plurality of electrodes), -ve electrode and + electrode to measure the changes in pH (see claims 1-17)."

Applicants disagree. As noted above, the claims require that the process step measure the electrical properties of the tissue sample. In very sharp contrast, the Parce et al. reference discusses only measuring secondary ionic properties of the fluid -- the "effects caused by the cell affecting agent". See column 3, lines 22 and following:

> "Preferred effects include the pH, Redox potential, and other electrical properties of the solution or suspension that flows in contact with the living cells in the microflow chamber, such as cell surface potential and trancellular potential."

Additionally at column 6, lines 22 and following:

> "Once stable, [fluid] flow in the chamber is halted and the silicon sensor signal is monitored. A decrease in potential reflects the decrease of pH in the chamber due to cellular metabolism. The rate of pH decreases is a measure of the metabolic rate of the cells."

At column 6, line 40 and following;

> "If one side is located upstream of the direction of flow from another and there are intervening cells, there will be a pH difference between the two sites with the upstream site being less acidic. This pH difference is due to the metabolic action of the cells on the medium as it traverses the space between the sites. The magnitude of the pH difference, as detected by the silicon semiconductor electrode, is a measure of the metabolic rate of the cells located between the two sites."

A similar discussion is had relating to cells which adhere to the surface of the flow chamber. Furthermore, each of the Examples speaks of detecting changes in metabolic rate. The disclosure in the body of the Parce et al. specification and in the Examples fails to show the measurement of "the electrical properties of the neural or muscle tissue sample". Each Parce et al disclosure shows and suggests only measurement of the secondary effect of some cellular activity, e.g., the metabolic rate.

There are many other differences between the procedure found in Parce et al and the claimed process. In addition to the difference mentioned just above, applicants would contend that Parce et al's collection of cells is not a "tissue" and specifically is not a "neural or muscle tissue sample." Consequently, it is clear that Parce et al does not anticipate the rejected claims. Similarly, there appears to be no reason why one of ordinary skill in the art would further consider the dispersed or aggregate cell masses described in the Parce et al. patent to render obvious neural or muscle tissue samples, nor would any teaching found therein suggest a process in which electrical activity in any sample is directly measured.

Withdrawal of the rejection is therefore believed to be completely appropriate.

35 U.S.C. § 102(b) - Giaever et al.

Claims 12, 14, and 16 stand rejected under 35 U.S.C. § 102(b) as anticipated by Giaever et al. (U.S. Patent No. 5,187,096). In support of the rejection, the Office Action notes:

> "Giaever et al describes a method which comprises a detector for detecting electrical properties of endothelial cells, fibroblast (examiner is viewing a collection of similar cells as tissue) when chemical substances thrombin is exposed to the cultures. (See column 3, lines 22-67). The invention has several application including testing the drugs. The prior art anticipates the claimed invention....."

Applicants respectfully disagree.

Applicants have responded to and, it was believed, overcome the rejection over Giaever in a response filed on September 24, 1999 in response to the Office Action dated March 24, 1999 (Paper No. 10). The argument made there that is quoted just below, is still appropriate here:

"Applicants disagree. The claimed device and procedure both require the use of a detector comprising a microelectrode array on a substrate, where the microelectrodes also operable as excitors, and the microelectrodes are suitable for use with a tissue sample. The Giaever et al. device is of a type that is not suitable for use with a tissue sample but instead is applicable only for a soup of cells. The quality of information relating to the electrical signal thus received is not in the same league as is derivable from the claimed device and procedure.

Let it be understood that no two electrodes of Giaever et al. are able to access a single slice of tissue."

Again, Applicants assert that the Giaever et al. disclosure is not drawn to the task of measuring electrical properties in a "neural or muscle tissue sample". Giaever et al. additionally lacks the specific active step of "contacting" a tissue sample with a plurality of electrodes. Giaever et al., instead, at best introduces a soup of individual cells into a measuring cell and therein grows or aglomerates a larger mass. There is no instance described in the Giaever et al. patent document in which anything approaching an aglomerate of cells is actively contacted with a microelectrode array.

Withdrawal of he rejection is requested.

35 U.S.C. § 103(a)

Claims 12, 14, and 16 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Nisch et al., (Biosense, Bioelect 1994, 9:737-741). In particular, the Office Action states:

"Nisch et al describes a method which comprises a detector for detecting electrical properties of neuronal activity in vitro (page 738-739). He measures a detectable electrical signal before and after stimulation in figure 7 which is observed (i.e. visible property). He further describes a testing device comprising electrical measurement portion (i.e., visible) visible detection portion (Figure 3-monitor, figure 4, figure 5, figure 6, etc)."

"Niche et al does not teach that the method used for tissues. However, Stedman's Medical Dictionary defines tissue as "a collection of similar

a neuronal or muscle tissue sample into the sample region, a step required by the claims under consideration.

Withdrawal of the rejection is respectfully requested.

CONCLUSION

Applicants have responded to each issue of substance raised in the Office Action. Allowance of the application is now requested. Should the Examiner have any additional comments, questions, or requests, she is invited to contact applicants' attorney at the number listed below. Should a personal or telephonic interview be desired, again, please contact applicants' attorney and accommodation will be made.

Respectfully submitted,

Dated: October 29, 2001 By: _____

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